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(54) **Title of the Invention: A Topical Skin Agent**

(57) **[Abstract]**

[Objective] To provide a topical skin agent that has superior effectiveness in color lightening and beautifying and whitening the skin in conditions of pigment deposition after sunburn, blotches, freckles and melasma and that is effective in the improvement of various types of skin diseases, skin roughness and chapping.

[Structure] A topical skin agent in which an extract of plants of the genus Alycia of the family Apocynaceae such as pulowaras (scientific name: Alycia reindwartii Bl.) is compounded.

[Claims]

[Claim 1] A topical skin agent in which an extract of plants of the genus Alycia of the family Apocynaceae is compounded.

[Claim 2] A topical skin agent as described in Claim 1 in which the plant of the genus Alycia of the family Apocynaceae is pulowaras (scientific name: Alycia reindwartii Bl.).

[Claim 3] A topical skin agent as described in Claim 1 or 2 which is a beautifying and whitening agent.

[Claim 4] A topical skin agent as described in Claim 1 which is a protease inhibitor.

[Claim 5] A topical skin agent as described in any one of Claims 1 to 4 in which the compounding quantity of the extract of plants of the genus Alycia of the family Apocynaceae is 0.005 to 20.0 parts by weight.

[Detailed Description of the Invention]

[0001]

[Field of Industrial Use] This invention relates to a topical skin agent in which an extract of a plant the genus Alycia of the family Apocynaceae is compounded, and, in greater detail, it relates to a topical skin agent that inhibits production of melanin, that is effective in the prevention and improvement of pigment deposition after sunburn and of blotches, freckles and melasma and that can be used for the improvement of contact dermatitis, psoriasis, pemphigus vulgaris and congenital pemphigus [NOTE: Japanese text may have an error here] in which changes in protease activity in the lesion are found and of other skin diseases such as dryness of the skin and chapping and as a hemostatic agent.

[0002]

[Prior art and problems the invention is intended to solve] There are a number of points about the mechanism of development of skin blotches and other conditions that are unclear. In general, it is thought that the pigment melanin is formed because of hormone abnormalities and stimulation by ultraviolet rays from sunlight and that abnormal deposition of it in the skin occurs. The pigment melanin, which is the cause of coloration of the skin, is produced in melanin producing granules (melanosomes) in the melanocytes that lie between the epidermis and the dermis and the melanin that is produced diffuses to adjacent cells as a result of osmotic action. The biochemical reaction that occurs in the melanocytes is presumed to be as follows. Specifically, the process of production of melanin pigment is a process in which tyrosine, which us an essential amino acid, is converted to dopaquinone by the action of the enzyme tyrosinase and in which it is changed to black-colored melanin via red pigment and colorless pigment by enzymatic or nonezymatic enzyme action. Consequently, inhibition of the action of tyrosinase, which is the first step of the reaction, is important in the inhibition of melanin production.

[0003] However, the compounds that inhibit the action of tyrosinase, except for hydroquinone, manifest their effects extremely slowly, for which reason their effectiveness in improvement of skin pigment deposition is insufficient. On the other hand, the effect of hydroquinone is manifested for a period of time. However, because sensitization occurs to it, its use is generally limited. Accordingly, in order to increase its safety, attempts have been made to convert it to a monoester of a higher fatty acid or to an alkyl monoether (Japanese Patent Application Early Disclosure No. 58-154507 [1983]). However, because esters are broken down by hydrolytic enzymes in the body, it is hard to say that they are safe. Further, ethers have not been found to be satisfactory in terms of safety.

[0004] In recent years, it is being ascertained that proteases are involved in the development of the morbid picture in various skin diseases. For example, in psoriasis, which is representative of keratotic diseases in which there are inflammatory abnormalities, high plasminogen activator (PA) activity is found in the affected epidermis. PA is a serine protease. Haustein reported that strong PA activity is present in particular in parakeratinized sites as psoriatic epidermis (Arch. Klin. Exp. Dermatol: 234, 1969). Fraki and Hopsu-Havu extracted PA activity from psoriatic scales using high concentration salt solutions (Arch. Dermatol. Res; 256, 1976). Further, It was ascertained in in vitro experimental systems that, in pemphigus vulgaris, PA, which is synthesized in large quantities in epidermal cells, converts plasminogen, which is present outside

cells, to plasmin, which digests intercellular binding substances, with the result that tissue fluid is retained between cells and that vesicles are formed in the epidermis (Morioka S. et al.: J. Invest. Dermatol ; 76, 1981). It is further thought that proteases play an important role in the process of the normal keratinization of the epidermis such as in the formation of the stratum corneum (Ogawa H., Yoshiike T.: Int. J. Dermatol : 23 (1984) and attempts are being made to use protease inhibitors for improving skin or as therapeutic agents for skin diseases.

[0005]

[Means for solving the problems] In the light of the circumstances described above, the inventors studied the effects of a wide range of substances in inhibiting melanin production as well as their protease inhibiting activity. As a result, they perfected this invention by discovering that extracts of plants of the genus Alycia of the family Apocynaceae have a melanin production inhibiting action and a protease inhibiting action. There have been no reports on the melanin production inhibiting action of plants of the genus Alycia of the family Apocynaceae and nothing whatsoever is known about their application in beautifying and whitening agents and as protease inhibitors. In addition, there are no instances of the compounding of extracts of plants of the genus Alycia of the family Apocynaceae in topical skin agents. The inventors perfected this invention on the basis of the information described above.

[0006] Specifically, this invention is a topical skin agent characterized in that an extract of plants of the genus Alycia of the family Apocynaceae is compounded in it.

[0007] We shall now present a detailed description of the structure of this invention. For example, Pulowaras (scientific name: Alycia reindwartii Bl.), is desirable as a plant of the genus Alycia of the family Apocynaceae that is used in this invention. It is a plant that grows in arid meadows and pastures in Indonesia. The extracts that are used in this invention are obtained by immersing the entire plant, including the leaves, bark and underground stems and fruit of the plant, in an extraction solvent and subjecting them to heating and reflux, after which the product is filtered and concentrated. Any extraction solvent may be used as long as it is a solvent that is ordinarily used in extraction. In particular, organic solvents including alcohols such as methanol and ethanol and acetone and ethyl acetate can be used individually or in combination.

[0008] The quantity of extract of the plant of the genus Alycia of the family Apocynaceae compounded in this invention is 0.005 to 20.0 weight %, and, preferably, 0.01 to 10.0 weight %, as dry matter in the total quantity of topical agent. When it is less than 0.005 weight %, the effect of this invention is not sufficiently manifested. When it exceeds 20.0 weight %, it is difficult to prepare the agent. This is not desirable. Moreover, there is no further increase in effect as the amount compounded increases over 10.0 weight %.

[0009] The topical skin agent of this invention may be applied as a beautifying-whitening agent or as a protease inhibitor. The term protease in the expression protease inhibitor is a general term for enzymes that catalyze the hydrolysis of peptide bonds. These proteases are classified into peptidases and proteinases. The former are enzymes that sever specific peptide bonds from the outside of the amino group terminals and the carboxyl group terminals of peptide chains. The latter, the proteinases, are divided into four general groups, serine systems, cysteine systems, aspartic acid systems and metal systems, depending on the type of active enzyme group and specific inhibitors present in them. The protease inhibitors in this invention are characterized in that they exhibit inhibitory activity specifically against serine proteases.

[0010] In addition to the aforementioned, components that are ordinarily used in topical skin agents such as cosmetic drug products and medicinal drug products, for example, other beautifying-whitening agents, moisturizing agents, antioxidants, oleaginous components, ultraviolet ray absorbents, surfactants, thickeners, alcohols, powdered components, colorants, aqueous components, water and various types of skin nutrients can be compounded appropriately as required in the skin topical agent of this invention.

[0011] In addition, metal blocking agents such as disodium edetate, trisodium edetate, sodium citrate, sodium polyphosphate, sodium metaphosphate and gluconic acid, drug preparations of caffeine, tannin, verapamil, tranexamic acid and derivatives thereof, licorice extracts, grabrizine [phonetic*], hot water extract of fire thorn fruit, various raw drugs, tocopherol

*[Translator's Note: Transliterated phonetically from the Japanese. As such, the spelling may differ from other transliterations.]

acetate and glycyrrhizinic acid and derivatives or salts thereof, beautifying-whitening agents such as vitamin C, magnesium ascorbate phosphate, ascorbic acid glucoside, arbutin and kojic acid and saccharides such as glucose, fructose, mannose, sucrose and trehalose can be compounded appropriately.

[0012] The topical skin agent of this invention may be any type of preparation as long as it is one conventionally used for topical skin agents, including, for example, an ointment, a cream, an emulsion, a lotion, a pack or a bathing agent.

[0013] Next we shall describe this invention in greater detail by means of examples. However, this invention is not limited by them. The quantities compounded are weight %. Prior to presenting the examples, we shall describe ①the melanin inhibiting effect, the tyrosinase inhibiting effect and the beautifying-whitening effect of the plant extracts of this invention and ②the method of testing for the protease inhibiting effect and the results thereof.

[0014] ① Methods of testing for melanin inhibiting effect, tyrosinase inhibiting effect and beautifying-whitening effect and results thereof

1. Preparation of Test Materials

50 g of bark of pulowaras was immersed for 1 week at room temperature in ethanol, the extract solution was concentrated and 2.18 g of ethanol extract was obtained. This extract was dissolved in 1% DMSO, the solution was diluted to adjust its concentration and the following tests were performed using this solution.

[0015] 2. Cell Culture Method

Cultured cells of B16 melanoma of mouse origin were used. They were cultured in Eagle's MEM culture medium containing 10% FBS and theophylline (0.09 mg/ml) at 37°C in a CO_2 incubator (95% air, 5% carbon dioxide). After culturing for 24 hours, test material solution was added to give a final concentration (converted concentration for dry extract) of 10^{-2} to 10^{-5} weight % and culturing was continued for an additional 3 days. Visual evaluations of the quantity of melanin production and determinations of tyrosinase inhibiting effect were made by the methods described below.

[0016] 3. Visual Determination of Melanin Quantity

A diffusion plate was placed on the cover of the well plate, the quantity of melanin inside the cells was observed with an invert microscope and a comparison was made with the case of a test material (reference) to which plant extract had not been added. Table 1 shows the results. As the reference example, the same test as described above was performed with Lamium sp. [dead nettle] (Labiatae, genus Lamium), which is known to have a melanin production inhibiting action. The results are also shown in Table 1. In the table, toxicity indicates cytotoxicity.

[0017] < Evaluation Criteria >

O: white (quantity of melanin)

Δ: somewhat white (quantity of melanin)

X: reference (quantity of melanin)

[0018] 4. Determination of Tyrosinase Activity

Before determination, the culture medium in the well was removed and washing was performed twice with 100μℓ of PBS. PBS containing 45μℓ of 1% Triton-X (brand name; surfactant manufactured by Rohm & Haas Company) was added to each well. The plate was agitated for 1 minute, with the cell membranes being thoroughly destroyed, absorbence at 475 nm was determined with a microplate reader and this value was taken as the absorbance at the time 0 minutes. Following that, 5μℓ of 10 mM L-Dopa solution was rapidly added, the sample was transferred to an incubator at 37°C and a reaction was carried out for 60 minutes. The plate was agitated for 1 minute and absorbance (475 nm) was determined at the time of 60 minutes. The amount of decrease in the difference in absorbance for the test material to which plant extract had been added relative to the difference in absorbance at 0 minutes and 60 minutes for the test material to which plant extract had not been added (control) was taken as the tyrosinase activity inhibition rate (%). The results are shown in Table 1. As the reference example, the same test as described above was performed for an ethanol extract of Lamium that had been found to have tyrosinase activity inhibiting action. These results are also shown in Table 1. In the table, toxicity indicates that cytotoxicity was found. The symbol - signifies that a significant difference at a level of significance of less than 5% was not found by comparison to the controls.

[0019]
[Table 1]

Test	Melanin production visual evaluation				Tyrosinase activity inhibition rate (%)			
Concentration (weight %)	10^{-5}	10^{-4}	10^{-3}	10^{-2}	10^{-5}	10^{-4}	10^{-3}	10^{-2}
Pulowaras extract	x	x	x	o	-	75	75	70
Lamium extract	x	x	x	x	-	-	-	55

[0020] 5. Beautifying-whitening Effect Test

[Test Method] Skin on the inner side of the upper arm of 40 subjects who had been exposed to summer sunlight for 4 hours (two hours a day, two days) was the object of the test. Each test material was applied once in the morning and evening over a four week period from day 5 after the day of exposure to the sunlight. The panel was divided into groups of 8 subjects, to give 5 groups and the tests were conducted with the formulation indicated below.

(Alcohol Phase)	
95% ethyl alcohol	55.0 weight %
Polyoxyethylene (25 mol) hardened castor oil ether	2.0
Antioxidant - preservative	suitable quantity
Fragrances	suitable quantity
Drug (shown in Table 2)	
(Aqueous Phase)	
Glycerol	5.0
Sodium hexametaphosphate	suitable quantity
Ion exchange water	Remainder

< Preparation Method > The aqueous phase and the alcohol phase were prepared separately, after which the two were mixed and solubilized.

[0021] Evaluation Method. The color lightening effect after use was evaluated on the basis of the following evaluation criteria.

< Evaluation Criteria >

◎: Case in which marked effectiveness and effectiveness was exhibited in more than 80% of the test subjects

O: Case in which marked effectiveness and effectiveness was exhibited in 50% to 80% of the test subjects

Δ: Case in which marked effectiveness and effectiveness was exhibited in 30% to 50% of the test subjects

X: Case in which marked effectiveness and effectiveness was exhibited in less than 30% of the test subjects

[0022] Test materials comprised of the compounding compositions indicated in the test methods described above and the whitening-beautifying effects as presented in Table 2 were compared. The results are shown in Table 2.

[0023]
[Table 2]

Drug	Compounded Amount (weight %)	Effectiveness
Nothing added	-	X
Hydroquinone	1.0	Δ
Pulowaras extract	0.1	O
Pulowaras extract	1.0	O
Pulowaras extract	10.0	◎

[0024] The pulowaras extracts in Table 2 were obtained by heating reduction of the bark of the plants in ethanol, after which the material was filtered, concentrated and dried.

[0025] As should be clear from Table 2, the effects after exposure to sunlight were found to be that addition of pulowaras extract prevented excessive deposition of melanin pigment and prevented development of black color.

[0026] ② Results of Test Method for Tyrosinase Inhibition Effect

Inhibitory activity on plasmin and trypsin as two representative serine proteases was evaluated.

[0027] 1. Preparation of Test Materials

The bark of pulowaras was immersed for 1 week in ethanol at room temperature and the extraction solution was concentrated and dried. The solid matter was again dissolved in ethanol and a 1% solution was made.

[0028] 2. Determination of Plasmin Inhibiting Activity

The inhibition rate % was found by the fibrin plate method. Specifically, a fibrin plate was prepared following the method of Astrup et al. (Arch. Biochem. : 40, 346, 1952) and test materials prepared as described above were diluted with ethanol to 0.1% and 0.01% for use. The results are shown in Table 3.

[0029] **Determination of Trypsin Inhibiting Activity** Inhibition rates were found following the method of Muramatu [NOTE: probably misprint for Muramatsu] et al. (J. Biochem.: 58, 214, 1965) using casein as the substrate. The test materials were similarly diluted to < 0.1% and 0.01% for use. The results are shown in Table 3. As reference examples, tests similar to that described above were performed on ethanol extracts of Kunyit (scientific name: Curcuma domestica) of the family Zingiberaceae and Lempuyang (scientific name: Zingiber aromaticum Mal.) of the family Zingiberaceae and mugwort, which are plants known to have been used for rough skin in the past. The results are also shown in Table 3.

[0030]
[Table 3]

	Inhibition Rate %	Concentration of Test Material Added	
		Plasmin	Trypsin
Pulowaras	0.1%	33.1	
	0.01%	27.5	
Kunyit	0.1%	3.0	
	0.01%	0	
Lempuyang	0.1%	0	
	0.01%	0	
Mugwort	0.1%	18.6	
	0.01%	5.8	

[0031]
Example 1, Cream

(Formulation)	
Stearic acid	5.0 weight %
Stearyl alcohol	4.0
Isopropyl myristate	18.0
Glycerol monostearic acid esters	3.0
Propylene glycol	10.0
Pulowaras methanol extract	0.01
Potassium hydroxide	0.2
Sodium hydrogensulfite	0.01
Preservative	suitable quantity
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Propylene glycol, pulowaras methanol extract and potassium hydroxide were added to and dissolved in ion exchange water and the solution was heated and maintained at 70°C (aqueous phase). The other constituents were mixed, fused by heating and maintained at 70°C (oleaginous phase). The oleaginous phase was gradually added to the aqueous phase, and, after addition of the total quantity had been completed, that temperature was maintained for a short period, with a reaction being brought about. Following that, it was uniformly emulsified with an homogenizer and was cooled to 30°C while it was being thoroughly stirred.

[0032]
Example 2; Cream

(Formulation)	
Stearic acid	2.0 weight %
Stearyl alcohol	7.0
Hydrogenated lanolin	2.0
Squalane	5.0
2-octyl dodecyl alcohol	6.0
Polyoxyethylene (25 mol) cetyl alcohol ether	3.0
Glycerol monostearic acid ester	2.0
Propylene glycol	5.0
Pulowaras ethanol extract	0.05
Sodium hydrogensulfite	0.03
Ethylparaben	0.3
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Propylene glycol was added to ion exchange water, heated and maintained at 70°C (aqueous phase). The other constituents were mixed, heated and fused and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase, preparatory emulsification and then uniform emulsification were performed with an homogenizer, after which the product was cooled to 30°C as it was being thoroughly stirred.

[0033]
Example 3; Cream

(Formulation)	
Solid paraffin	5.0 weight %
Beeswax	10.0
Vaseline	15.0
Liquid paraffin	41.0
Glycerol monostearic acid ester	2.0
Polyoxyethylene (20 mol) sorbitan monolauric acid ester	2.0
Soap powder	0.1
Borax	0.2
Pulowaras acetone extract	0.01
Sodium hydrogensulfite	0.03
Ethylparaben	0.3
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Soap powder and borax were added to the ion exchange water and they were heated, fused and maintained at 70°C (aqueous phase). The other constituents were mixed, heated and fused and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase as the materials were being stirred and a reaction was performed. After the reaction was completed, the product was uniformly emulsified with an homogenizer. After emulsification, it was cooled to 30°C as it was being stirred.

[0034]

Example 4; Emulsion

(Formulation)	
Stearic acid	2.5 weight %
Cetyl alcohol	1.5
Vaseline	5.0
Liquid paraffin	10.0
Polyoxyethylene (10 mol) monooleic acid ester	2.0
Polyethylene glycol 1500	3.0
Triethanolamine	1.0
Carboxyvinyl polymer	0.05
(brand name: Carbopol [phonetic], B.F.Goodrich Chemical Company)	
Pulowaras ethyl acetate ester extract	0.01
Sodium hydrogensulfite	0.01
Ethylparaben	0.3
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Carboxyvinyl polymer was dissolved in a small quantity of ion exchange water (Phase A). Polyethylene glycol 1500 and triethanolamine were added to the remaining ion exchange water and they were heated and fused and maintained at 70°C (aqueous phase). The other constituents were heated and fused and maintained at 70°C (oleaginous phase). The oleaginous phase was added to the aqueous phase and preliminary emulsification was performed. Phase A was added and uniform emulsification was performed with an homogenizer. After emulsification, the product was cooled to 30°C as it was being stirred.

[0035]

Example 5; Emulsion

(Formulation)	
Microcrystlline wax	1.0 weight %
Beeswax	2.0
Lanolin	20.0
Liquid paraffin	10.0
Squalane	5.0
Sorbitan sesquioleic acid ester	4.0
Polyoxyethylene (20 mol) sorbitan monooleic acid ester	1.0
Propylene glycol	7.0
Pulowaras acetone extract	10.0
Sodium hydrogensulfite	0.01
Ethylparaben	0.3
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Propylene glycol was added to the ion exchange water, heated and maintained at 70°C (aqueous phase). The other constituents were mixed and heated and fused and maintained at 70°C (oleaginous phase). Water was gradually added as the oleaginous phase was being stirred and uniform emulsification was performed with an homogenizer. After emulsification, the product was cooled to 30°C as it was being stirred.

[0036]

Example 6; Jelly

(Formulation)	
95% Ethyl alcohol	10.0 weight %
Dipropylene glycol	15.0
Polyoxyethylene (50 mol) oleyl alcohol ether	2.0
Carboxyvinyl polymer	1.0
(brand name: Carbopol 940, B.F. Goodrich Chemical Company)	
Sodium hydroxide	0.15
L-arginine	0.1
Pulowaras 50% ethanol aqueous solution extract	7.0
Sodium 2-hydroxy -4-methoxybenzophenone sulfonate	0.05
Ethylenediamine tetraacetate trisodium 2-hydrate	0.05
Methylparaben	0.2
Fragrances	suitable quantity
Ion exchange water	remainder

(Preparation Method) Carbopol 940 was dissolved uniformly in ion exchange water. Separately, pulowaras 50% ethanol aqueous solution extract and polyoxyethylene (50 mol) oleyl alcohol ether were dissolved in 95% ethanol and the solution was added to the aqueous phase. Next, the other constituents were added, after which neutralization and thickening were effected in sodium hydroxide and L-arginine.

[0037]
Example 7; Beauty Solution

(Formulation)	
(Phase A)	
Ethyl alcohol (95%)	10.0 weight %
Polyoxyethylene (20 mol) octyl dodecanol	1.0
Pantothenyl ethyl ether	0.1
Pulowaras methanol extract	1.5
Methylparaben	0.15
(Phase B)	
Potassium hydroxide	0.
(Phase C)	
Glycerol	5.0
Dipropylene glycol	10.0
Sodium hydrogensulfite	0.03
Carboxyvinyi poiymer	0.2
(brand name: Carbopol 940, B.F. Goodrich Chemical Company)	
Purified water	remainder

(Preparation Method) Phase A and phase C were dissolved uniformly and phase A was added to phase C and solubilized. Next, phase B was added, after which filling was performed.

[0038] Example 8; Pack

(Formulation)	
(Phase A)	
Dipropylene glycol	5.0 weight %
Polyoxyethylene (60 mol) hardened castor oil	5.0
(Phase B)	
Pulowaras methanol extract	0.01
Olive oil	5.0
Tocopherol acetate	0.2
Ethylparaben	0.2
Fragrances	0.2
(Phase C)	
Sodium hydrogen sulfite	0.03
Polyvinyl alcohol	13.0
(degree of saponification, 90; degree of polymerization, 2,000)	
Ethanol	7.0
Purified water	remainder

(Preparation Method) Phase A, phase B and phase C were dissolved uniformly and phase B was added to phase A and solubilized. Next, this product was added to phase C, after which filling was performed.

[0039] Example 9; Solid foundation

(Formulation)	
Talc	43.1 weight %
Kaolin	15.0
Sericite	10.0
Zinc white	7.0
Titanium dioxide	3.8
Yellow iron oxide	2.9
Black iron oxide	0.2
Squalane	8.0
Isostearic acid	4.0
Monooleic acid POE sorbitan	3.0
Isocetyl octanoate	2.0
Pulowaras ethanol extract	1.0
Preservative	suitable quantity
Fragrances	suitable quantity

(Preparation Method) The powdered constituents from the talc to the black iron oxide were thoroughly mixed with a blender, the oleaginous constituents from squalane to isocetyl octanoate, the pulowaras ethanol extract, the preservative and the fragrances were added and thoroughly kneaded in, after which filling and molding were performed.

[0040]
Example 10; Emulsified foundation (cream type)

(Formulation)	
(Powder components)	
Titanium dioxide	10.3 weight %
Sericite	5.4
Kaolin	3.0
Yellow iron oxide	0.8
Red iron oxide	0.3
Black iron oxide	0.2
(Oleaginous phase)	
Decamethyl cyclopentasiloxane	11.5
Liquid paraffin	4.5
Polyoxyethylene modified dimethyl polysiloxane	4.0
(Aqueous phase)	
Purified water	50.0
1,3-butylene glycol	4.5
Pulowaras ethanol extract	1.5
Sorbitan sesquioleic acid ester	3.0
Preservative	suitable quantity
Fragrances	suitable quantity

(Preparation Method) The aqueous phase was heated and stirred, after which the powered constituents, which had been thoroughly nixed and pulverized, were added and the mixture was treated with an homogenizer. The oleaginous phase, which had been heated and mixed, was added and was treated with an homogenizer, after which the fragrances were added as the mixture was being stirred and was then cooled to room temperature.

[0041]

[Effect of the Invention] As has been described above, it is anticipated that the topical skin agent of this invention has a melanin production inhibiting action and a tyrosinase activity inhibiting action, that it has superior effects in color lightening and beautifying-whitening of pigment deposition after sunburn, blotches, freckles and melasma, that it has a superior protease inhibiting action and that it has superior effects in improvement of various skin diseases, rough skin and chapping.

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